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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)

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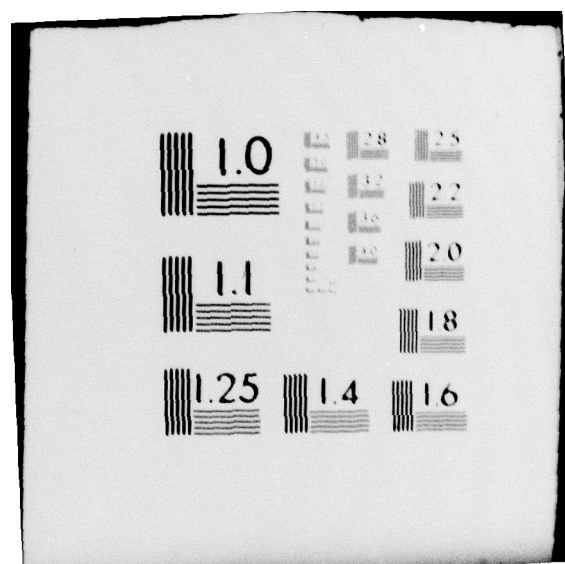
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

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TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENTS AI3-36439, AI3-36440, AND AI3-36466
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NUMBERS 75-51-0896-79, 75-51-0897-79, AND 75-51-0898-79
MAY 1976 - JUNE 1979,

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0896-79 thru 75-51-0898-79	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-36439, AI3-36440, and AI3-36466, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0896-79, 75-51-0897-79, and 75-51-0898-79, May 1976 - June 1979		5. TYPE OF REPORT & PERIOD COVERED Final, May 76 - Jun 79
7. AUTHOR(s) ALLEN W. SINGER, CPT, VC		6. PERFORMING ORG. REPORT NUMBER 1979
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010		8. CONTRACT OR GRANT NUMBER(s)
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Fort Sam Houston, TX 78234		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		12. REPORT DATE May 76 - Jun 79
		13. NUMBER OF PAGES 6
		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Topical Hazard Evaluation photoirritation USDA Proprietary Chemicals skin irritation AI3-36439 candidate repellents AI3-36440 AI3-36466		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Hazard evaluations of AI3-36439, AI3-36440, and AI3-36466 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compounds produced a photoirritation reaction in all rabbits tested, and caused slight primary skin irritation. They did not, however, cause any eye irritation in rabbits or sensitize guinea pigs. They did not demonstrate an acute ingestion hazard in rats.		

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Singer/jg/AUTOVON
584-3980

HSE-LT-T/WP

17 AUG 1979

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
AI3-36439, AI3-36440, and AI3-36466, US Department of Agriculture
Proprietary Chemicals, Study Nos. 75-51-0896-79, 75-51-0897-79, and
75-51-0898-79, May 1976 - June 1979

Executive Secretary
Armed Forces Pest Control Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

Hazard evaluations of AI3-36439, AI3-36440, and AI3-36466 were performed by means of laboratory animal studies using rats, rabbits, and guinea pigs. The technical grade compounds produced a photoirritation reaction in all rabbits tested, and caused slight primary skin irritation. They did not, however, cause any eye irritation in rabbits or sensitize guinea pigs. They did not demonstrate an acute ingestion hazard in rats. It was recommended that AI3-36439, AI3-36440, and AI3-36466 not be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

BRENDAN E. JOYCE, Ph.D.
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ABERDEEN PROVING GROUND, MARYLAND 21010

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TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENTS AI3-36439, AI3-36440, AND AI3-36466
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NUMBERS 75-51-0896-79, 75-51-0897-79, AND 75-51-0898-79
MAY 1976 - JUNE 1979

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, Florida, 5 May 1976.

b. Memorandum of Understanding between the Department of the Army, Office of The Surgeon General; the US Army Health Services Command; the US Army Environmental Hygiene Agency; the Armed Forces Pest Control Board, and the US Department of Agriculture, effective 1970 with Amendment No. 1 effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, USAEHA, 1972, revised 1976.

3. PURPOSE. The purpose of this study is to provide guidance for further entomological testing of the candidate insect repellents AI3-36439, AI3-36440, and AI3-36466.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellents AI3-36439, AI3-36440, and AI3-36466, USDA Proprietary Chemicals, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows:*†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education, and Welfare Publication No. (NIH) 74-23, revised in 1972, and in 1978.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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Topical Hazard Eval Study Nos. 75-51-0896-79, 75-51-0897-79, and 75-51-0898-79, May 76-Jun 79

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
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SKIN IRRITATION STUDIES

Rabbits

Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	All three compounds produced mild primary irritation of the intact skin and to the skin surrounding an abrasion in all rabbits.	USAEHA Category II (ref Appendix)
0.5 ml technical grade compound applied to each of six rabbits.		

EYE IRRITATION STUDIES

Rabbits

Single 24-hour application of 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	Compounds AI3-36439, AI3-36440 and AI3-36466 did not produce any injury to the cornea and no injury to the conjunctiva in 6 out of 6 rabbits.	USAEHA Category A (ref Appendix)
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APPROXIMATE LETHAL DOSE (ALD)

Oral

Rats (male) - no diluent	ALD >7400 mg/kg for all three compounds.	Presents little lethal hazard from accidental ingestion.
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Topical Hazard Eval Study Nos. 75-51-0896-79, 75-51-0897-79, and 75-51-0898-79, May 76-Jun 79

Test	Results	Interpretation
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PHOTOCHEMICAL SKIN IRRITATION STUDIES

Rabbits

A single application (0.05 ml) of a 25 percent (w/v) solution of the compounds and of a 10 percent (w/v) oil of Bergamot solution (positive control) in 95 percent ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	25 percent solutions of AI3-36439, AI3-36440, and AI3-36466 in ethanol caused greater irritant effects in irradiated areas than in unirradiated skin areas. Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.	All compounds caused photochemical irritation reactions on rabbits and may cause a similar irritation in humans.
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Control

Following UV exposures of the rabbits 0.05 ml of test compounds, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.

Topical Hazard Eval Study Nos. 75-51-0896-79, 75-51-0897-79, and 75-51-0898-79, May 76-Jun 79

Test	Results	Interpretation
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SENSITIZATION STUDIES

Guinea Pigs

Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36439, AI3-36440, AI3-36466, or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.

Ten test guinea pigs received ten sensitizing doses of either AI3-36439, AI3-36440, or AI3-36466 and were challenged after 2 weeks' rest with a 0.1 percent solution of the respective candidate repellent.

Challenge dose of test repellents did not produce sensitization reactions.

Compounds AI3-36439, AI3-36440, and AI3-36466 did not produce sensitization reactions under test conditions, and are not expected to produce sensitization reactions in man.

Ten positive control guinea pigs received ten sensitizing doses of DNCB, and were challenged after 2 weeks' rest with a 0.1 percent solution of DNCB.

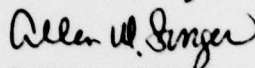
Positive controls (DNCB) produced a marked sensitization reaction in 10 of 10 guinea pigs.

* A known skin sensitizer.

Topical Hazard Eval Study Nos. 75-51-0896-79, 75-51-0897-79, and 75-51-0898-79, May 76-Jun 79

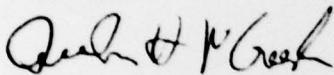
5. CONCLUSION. Compounds AI3-36439, AI3-36440, and AI3-36466 have potential for causing a photochemical irritation reaction in humans and do not qualify as nonhazardous insect repellents.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1b), it is recommended that AI3-36439, AI3-36440, and AI3-36466, USDA Proprietary Chemicals, not be approved as candidate insect repellents.



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APPENDIX

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.